

separate petition accompanies this amendment. Claims 1-10 are currently under examination.

I. Amendment

Claim 4 has been amended to remove the phrase for use in forming a plurality of small molecules with different chemical sequences.

No new matter has been added by these amendments.

Also attached is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"Version with Markings to Show Changes Made."**

II. Rejection Under 35 U.S.C. §112, first paragraph

Claims 1-10 were rejected under 35 U.S.C. §112, first paragraph as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention without undue experimentation.

This rejection has already been addressed in the previous Office action response.

III. Rejection Under 35 U.S.C. §112, second paragraph

Claims 1-5 and 8-10 were rejected under 35 U.S.C. §112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. These rejections are traversed in view of the following.

A. "nucleic acid tags"

In claim 1, the term "nucleic acid tags" has been rejected as not providing one of ordinary skill in the art a mean of determining the metes and bounds of the claimed method. The Examiner asserts that it is not clear if the term encompasses an additional, unrecited term that has been described in the specification -- "oligonucleotide analogs".

The specification, on page 9, lines 14-16, defines a nucleic acid tag to mean "the nucleic acid sequences which comprise a plurality of different first hybridization sequences, a mixture of different second hybridization sequences, and a chemical reaction site. Such 'nucleic acid tags' are capable of directing the synthesis of the combinatorial library of the present invention ..."

An oligonucleotide analog is defined as "a nucleic acid that has been modified and which is capable of some or all of the chemical or biological activities of the oligonucleotide from which

it was derived."

Thus, in response to the Examiner's inquiry, an oligonucleotide analog may be a nucleic acid tag if it: (i) is a nucleic acid that has been modified and which is capable of some or all of the biological activities of the oligonucleotide from which it was derived; and (ii) includes a plurality of different first hybridization sequences, a mixture of different second hybridization sequences, and a chemical reaction site.

**B. "chemical reaction site"**

In claims 1 and 9, the term "chemical reaction site" has been rejected as not providing one of ordinary skill in the art a means of determining the metes and bounds of the claimed invention. The Examiner asserts that the term is indefinite because the specification defines the term as a chemical component capable of forming a variety of chemical bonds, and that any "'component' of any compound is 'capable of forming a variety of chemical bonds.'"

This rejection has already been addressed in the previous Office action response.

**C. Reagents**

The Examiner has rejected claim 1 as lacking clarity, asserting that it is not clear whether only one (i.e., the same) reagent is reacted with all of the tags within a subset or if more than one reagent may be reacted with the tags within a subset, as long as each tag reacts with only one reagent.

Neither of the Examiner's interpretations is consistent with the language of claim 1. For example, step (b) of claim 1 requires that a first selected reagent is reacted with the chemical reaction sites in each of the subsets. A reagent-specific compound intermediate is thereby formed on the associated sequence in each subset. Thus, although one reagent certainly reacts with the chemical reaction sites in each subset, there is no requirement in the claim that "only one" reagent react.

**D. "oligonucleotide analog"**

The Examiner has rejected this term in claim 2 as not providing a means for determining the metes and bounds of the claim. The Examiner asserts that the definition of the term "oligonucleotide analog" is too broad and that base-pairing may be considered a physical, rather than biological property.

The term "oligonucleotide analog", as defined on page 8, lines 20-23 of the specification,

means "a nucleic acid that has been modified and which is capable of some or all of the chemical or biological activities of the oligonucleotide from which it was derived."

First, as stated by the CCPA, "[a]n applicant is entitled to claims as broad as the prior art and his disclosure will allow." *In re Rasmussen*, 650 F.2d 1212, 211 USPQ 323, 326 (C.C.P.A. 1981). The breadth of a claim is not to be equated with indefiniteness. *In re Miller*, 441 F.2d 689, 169 USPQ 597, 600 (C.C.P.A. 1971). Thus, the Examiner may not reject claim 2 as indefinite merely because it is broad.

Second, the Examiner's concern that base-pairing may be considered a physical, rather than biological, property is irrelevant. Claim 2 requires that the surface bound oligonucleotide or oligonucleotide analog be capable of forming base-specific duplexes with one of the hybridizing sequences. Thus, an oligonucleotide analog must have base-pairing capabilities to be encompassed within claim 2, but whether base-pairing is considered a physical or biological property has no impact whatsoever.

E. "subunit oligomers"

In claim 3, the phrase "for use in forming a plurality of oligomers with different subunit sequences" has been rejected as being too broad, because, the Examiner asserts, "it is clear that nucleic acids and peptides are encompassed by the claim, but [it] is not possible to determine what other types of molecules are included or excluded from the scope of the claim."

This rejection has already been addressed in the previous Office action response.

F. "small molecules"

In claim 4, the term "small molecules" has been rejected as not being clear with regard to the metes and bounds of the claim.

Claim 4 has been amended to remove the term "small molecules" thereby obviating the rejection.

G. "small molecules with different chemical sequences"

In claim 4, the term "small molecules with different chemical sequence" has been rejected by the Examiner as being "difficult to interpret."

Claim 4 has been amended to remove the term "small molecules with different chemical sequences" thereby obviating the rejection.

H. Claims 1 and 5 have been rejected as being incomplete for omitting structural cooperative relationships of elements. Specifically, the Examiner asserts that the relationships between the sequences in the nucleic acid tags and the reactions that result in the directed synthesis of a plurality of compounds are omitted.

Claim 1 requires that a first reagent reacts with chemical reaction sites in the first group of subsets of nucleic acid tags formed in step (a). In each subset, a selected first hybridization sequence is common to all of the nucleic acid tags. As noted in step (b), a reagent-specific compound intermediate is formed on the associated sequence in each subset. This is repeated in steps (c) and (d) for a second hybridization sequence and a second reagent. Thus, the hybridization sequences in the nucleic acid tags, as explicitly in step (d), are directing the synthesis of the compounds. No relationships between the sequences in the tags and the reactions that result are omitted.

And, as noted in the previous office action response, the specification also provides guidance. In rejecting a claim under Section 112, second paragraph, an Examiner must establish that one of ordinary skill in the pertinent art, when reading the claim in light of the supporting specification, would not have been able to ascertain with a reasonable degree of precision and particularity the specific area set out and circumscribed by the claim. *Ex parte Wu*, 10 USPQ 2d 2031, 2033 (B.P.A.I. 1989); *In re Moore*, 439 F.2d 1232, 169 USPQ 236, 238 (C.C.P.A. 1971); *In re Hammack*, 427 F.2d 1378, 166 USPQ 204, 208 (C.C.P.A. 1970). In the instant case, the specification provides ample guidance as to the relationships between the elements in the claims. The Examiner is particularly directed to Fig. 1, which provides a visual representation which may be used to clarify the relationships of the recited claim elements.

It is well settled that the "language of the claims, read in light of the specification" is to be considered when determining whether the claims are definite. *Allen Archery Inc. v. Browning Mfg. Co.*, 819 F.2d 1087, 2 USPQ 2d 1490, 1494 (Fed. Cir. 1987). The definiteness of the language employed must be analyzed not in a vacuum, but in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. *In re Angstadt*, 537 F.2d 498, 190 USPQ 214, 217 (C.C.P.A. 1976) (quoting *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (C.C.P.A. 1971)). The law is clear that "if the claims, read in the light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more." *North Am. Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 28 USPQ 2d 1333, 1339 (Fed. Cir.

1993). The drawings may be used in the same way as the written specification to provide evidence relevant to claim interpretation. *Autogiro Co. of Am. v. United States*, 384 F.2d 391, 398, 155 USPQ 697, 703 (Ct. Cl. 1967).

Because the Examiner has not established that the claims are not ascertainable to one of skill in the art in view of the specification, Applicants submit that the rejection is improper.

I. "yield a subpopulation of nucleic acid tags"

Claim 8 has been rejected for not being clear. The Examiner states, "[t]he rejection is over the question as to whether or not the subpopulation [of] nucleic acid tags to be used to carry out the method of claim 1 still have synthesized compounds attached or what method steps might be used to *"yield a subpopulation of nucleic acid tags."*

First, as stated in the previous Office action response and the specification on page 16, line 33 – page 17, line 3, there is no requirement that the synthesized compounds be detached from the nucleic acid tags. Second, with regard to what method steps might be used to yield a subpopulation of nucleic acid tags, claim 8 states that the subpopulation is enriched by identifying one or more compounds having a desired activity. This identification step is what is used to yield the subpopulation.

An exemplary selection and identification method is described in the specification. Page 16, line 33 – page 17, line 3 describe how a compound library is screened for a desired activity such as the ability to catalyze a particular reaction or to bind with high affinity to an immobilized receptor. "In most cases, the subpopulation of molecules with the desired activity, as well as their nucleic acid tags, are physically partitioned away from siblings during the selection. Following selection, the nucleic acid tags attached to the selected molecules are amplified by polymerase chain reaction ..."

It is well settled that the "language of the claims, read in light of the specification" is to be considered when determining whether the claims are definite. *Allen Archery Inc. v. Browning Mfg. Co.*, 819 F.2d 1087, 2 USPQ 2d 1490, 1494 (Fed. Cir. 1987). The definiteness of the language employed must be analyzed not in a vacuum, but in light of the teachings of the prior art and of the particular application disclosure as it would be interpreted by one possessing the ordinary level of skill in the pertinent art. *In re Angstadt*, 537 F.2d 498, 190 USPQ 214, 217 (C.C.P.A. 1976) (quoting *In re Moore*, 439 F.2d 1232, 1235, 169 USPQ 236, 238 (C.C.P.A. 1971)). The law is clear that "if the claims, read in the light of the specification, reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the

language is as precise as the subject matter permits, the courts can demand no more." *North Am. Vaccine, Inc. v. American Cyanamid Co.*, 7 F.3d 1571, 28 USPQ 2d 1333, 1339 (Fed. Cir. 1993).

Because the Examiner has not established that the claim is not ascertainable to one of skill in the art in view of the specification, Applicants submit that the rejection is improper.

J. "adding a chemical reaction site"

Claims 9 and 10 have been rejected as being incomplete for omitting method steps that provide a means for adding a chemical reaction site.

The Office action lists this rejection as being withdrawn on page 2 under "Withdrawn Rejections" and maintained on page 8 under "Maintained Rejections."

This rejection has already been addressed in the previous Office action response.

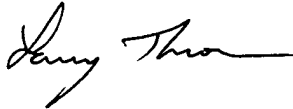
Accordingly, Applicants respectfully request withdrawal of the rejections under 35 U.S.C. §112, second paragraph.

IV. Conclusion

In view of the above amendments and remarks, Applicants submit that the pending claims are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4405.

Respectfully submitted,



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**Version with Markings to Show Changes Made**

**In the Claims:**

Claim 4 has been amended as follows:

4. (Amended) The method of claim 1, ~~for use in forming a plurality of small molecules with different chemical sequences,~~ wherein each of said reacting steps includes adding a selected chemical substituent to each of the subsets of nucleic acid tags under conditions effective to add that substituent to the chemical reaction site or last-added substituent carried thereon.